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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/673,168	11/28/2000	Roald Skurtveit	NIDN-10370	2221

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EXAMINER	
SHARAREH, SHAHNAM J	
ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 08/21/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Offic Action Summary	Application No. 09/673,168	Applicant(s) SKURTVEIT ET AL.	
	Examiner Shahnam Sharareh	Art Unit 1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Peri d f r Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11/28/2000, 4/23/2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's election with traverse of phosphatidylserine-stabilized perfluorobutane and sodium dodecyl sulphate in Paper No. 9B has been acknowledged. The traversal is on the grounds that Examiner has misinterpreted the role of stabilizing agents and destabilizing agents in the claimed invention. In response, Examiner states Applicant has misunderstood the election requirment. As stated in Page 3 of the requirement, the stabilizing agent of claims 5-8 encompass "various chemical moieties." Therefore, Examiner has viewed, for example, a filmogenic protein to be a patentably distinct species from a surfactant comprising phospholipid. Similarly, the destabilizing agents set forth in claims 11-12 are of different chemical moieties, which are viewed to be patentably distinct. Since, Applicants have not provided any evidence or admitted on the record that the species are obvious variations of each other, the election of species requirement is proper. The opposing role of stabilizing agent and destabilizing agents in the instant claims is not a relavent to the requirement.

The Applicant also raises the question that the Examiner is not entitled to raise a non-unity objection once the issue has been described in the international phase. In response, the Applicant's attention is drawn to MPEP 1893.03 (d), U.S. National Application Filed Under 35 U.S.C. 371. § 1.499 *Unity of invention during the national stage*. Accordingly:

> If the examiner find that a national stage application lacks unity of invention under § 1.475, the examiner may in an Office action require the applicant in the response to that action to elect the invention to which the claims shall be restricted. Such requirement may be made before any action on the merits but may be made at any time before the final action at the discretion of the examiner. Review of any such requirement is provided under § § 1.143 and 1.144.

Subsequently, the search is directed to the elected species and their respective subgenus of phospholipids and alkyl sulphates.

Claim Rejections - 35 USC 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

2. Claims 21-22 are is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966). Claims 21-22 provide for the use of the composition of instant claim 1, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass.

Specification

Content of Specification

(a) Title of the Invention: See 37 CFR 1.72(a) and MPEP § 606. The title of the invention should be placed at the top of the first page of the specification unless the title is provided in an application data shet. The title of the invention should be brief but technically accurate and descriptive, preferably from two to seven words may not contain more than 500 characters.

(b) Cross-References to Related Applications: See 37 CFR 1.78 and MPEP § 201.11.

(c) Background of the Invention: See MPEP § 608.01(c). The specification should set forth the Background of the Invention in two parts:

(1) Field of the Invention: A statement of the field of art to which the invention pertains. This statement may include a paraphrasing of the applicable U.S. patent classification definitions of the subject matter of the claimed invention. This item may also be titled "Technical Field."

(2) Description of the Related Art including information disclosed under 37 CFR 1.97 and 37 CFR 1.98: A description of the related art known to the applicant and including, if applicable, references to specific related art and problems involved in the prior art which are solved by the applicant's invention. This item may also be titled "Background Art."

(d) Brief Summary of the Invention: See MPEP § 608.01(d). A brief summary or general statement of the invention as set forth in 37 CFR 1.73. The summary is separate and distinct from the abstract and is directed toward the invention rather than the disclosure as a whole. The summary may point out the advantages of the invention or how it solves problems previously existent in the prior art (and preferably indicated in the Background of the Invention). In chemical cases it should point out in general terms the utility of the invention. If possible, the nature and gist of the invention or the inventive concept should be set forth. Objects of the invention should be treated briefly and only to the extent that they contribute to an understanding of the invention.

(e) Brief Description of the Several Views of the Drawing(s): See MPEP § 608.01(f). A reference to and brief description of the drawing(s) as set forth in 37 CFR 1.74.

(f) Detailed Description of the Invention: See MPEP § 608.01(g). A description of the preferred embodiment(s) of the invention as required in 37 CFR 1.71. The description should be as short and specific as is necessary to describe the invention adequately and accurately. Where elements or groups of elements, compounds, and processes, which are conventional and generally widely known in the field of the invention described and their exact nature or type is not necessary for an understanding and use of the invention by a person skilled in the art, they should not be described in detail. However, where particularly complicated subject matter is involved or where the elements, compounds, or processes may not be

commonly or widely known in the field, the specification should refer to another patent or readily available publication which adequately describes the subject matter.

(g) Claim or Claims: See 37 CFR 1.75 and MPEP § 608.01(m). The claim or claims must commence on separate sheet (37 CFR 1.52(b)). Where a claim sets forth a plurality of elements or steps, each element or step of the claim should be separated by a line indentation. There may be plural indentations to further segregate subcombinations or related steps. See 37 CFR 1.75 and MPEP § 608.01(i)-(p).

(h) Abstract of the Disclosure: See MPEP § 608.01(f). A brief narrative of the disclosure as a whole in a single paragraph of 150 words or less commencing on a separate sheet following the claims. In an international application which has entered the national stage (37 CFR 1.491(b)), the applicant need not submit an abstract commencing on a separate sheet if an abstract was published with the international application under PCT Article 21. The abstract that appears on the cover page of the pamphlet published by the International Bureau (IB) of the World Intellectual Property Organization (WIPO) is the abstract that will be used by the USPTO. See MPEP § 1893.03(e).

3. In the instant case, priority information is not cross refereneced. The headings for each section of the specification are missing and no abstract is submitted.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites a "a combined presentation" which appears to be a typographic error. Correction is requested.

Claim 2 recites the limiations "a ketone, an ester or a mixture of any of the foregoing," which renders the scope of the claim ambiguous. It is not clear whether the ketone or the ester are such derivatives of the optionally halogenated low molecular weight hydrocarbone or a simply "any ketone" or "any ester" or "any mixture of such compounds." Clarification is requested.

Claim 5 recitation of "an initially coalescence-resisting surface membrane,.." renders the scope of the claim ambiguous. It is not clear what compounds encompass "an initially coalescence-resisting surface membrane."

In claims 11-12, the recitation of "selected from... and" is an improper Markush language. Applicant is encouraged to use proper Markush language. Alternative expressions are permitted if they present no uncertainty or ambiguity with respect to the question of scope or clarity of the claims. When materials recited in a claim are so related as to constitute a proper Markush group, they may be recited in the conventional manner, or alternatively. For example, if "wherein R is a material selected from the group consisting of A, B, C and D" is a proper limitation, then "wherein R is A, B, C or D" shall also be considered proper. See MPEP 2173.

Claims 21-22 provides for the use of the composition of instant claim 1, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 1-22 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-32 of U.S. Patent No. 6,375,931. Although the conflicting claims are not identical, they are not patentably distinct from each other because the patented claims are directed to combined preparations comprising gaseous emulsions, destabilizing agents, a vasodilator and methods of use thereof, wherein the gas is a perfluorocarbon. The scope of the patented claims significantly overlaps with those of the pending claims, except that their diffusible component is capable of penetrating inside dispersed gas to provide controlled growth thereof. However, it would have been obvious to one of ordinary skill in the art at the time of invention to practice the instantly claimed invention, because all the pending claims use the same diffusible components thus providing the similar effects as of the diffusible components of the patented claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

6. Claims 1-13, 15-19, 21-22 are rejected under 35 U.S.C. 102(e) as being anticipated by Unger US Patent 5,846,517(Unger I).

Unger discloses coadministeration of compositions comprising gaseous liposomes dispersions and a vasodilator such as enalapril (abstract; col 49-line 55, col 50-line67; examples 1-4; col 55, lines 1-30). Unger uses various types of phospholipids including phosphopatic acid or phosphatidylglycerol (see example 1; col 61, lines 25-55). Unger also discloses the use of perfluorobutane (col 62, lines 40-41). Unger further discloses the use of stabilizers such as polyethylene glycols and emulsifying agents such as sodium lauryl sulfate (an alkyl sulphate)

in his compositions (col 27-29). Accordingly, Unger anticipates the limitations of the instant claims.

7. Claims 1-12, 15-18, 21-22 are rejected under 35 U.S.C. 102(e) as being anticipated by Unger US Patent 5,733,572 (Unger II).

Unger II discloses phospholipid bound gaseous contrast medium comprising a phospholipid including phosphatidylserine, a perfluorocarbon gas in an aquesou medium comprising sodium chloride, propylene glycol and sodium dodecyl sulfate and methods of use thereof in combination with a therapeutic agent such as a radioactive particle(see examples 10 and 26; col 58, lines 28-67; col 61, line 20; col 66, line 34). Thus, Unger II anticipates the limitations of the instant claims.

8. Claims 1-22 are rejected under 35 U.S.C. 102(e) as being anticipated by Ostensen et al US Patent 6,375,931 (Ostensen).

Ostensen discloses preparations comprising gaseous microbubbles in combination with a vasodilator such as adenosine to enhance the signal intensity during ultrasound imaging procedure (see abstract). WO '324 discloses perfluorobutane-filled micorbubbles encapsulated by phospholipid moieties such as phosphatidylserine (examples 1, 5-11; claims 1-32). Thus, Ostensen anticipates the limitations of the instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Unger II.

Unger's teachings are described above. Unger does not teach the use of adenosine as a vasodilator, but indicates that various cardiovascular agents such as nitoglycerin, nicardipine or propanolol which all cause peripheral

vasodilatations. In fact, Unger teaches that drugs such as adenosine can be modified in the form of prodrugs in order to assert their activities (see col 25, lines 29-37). Accordingly, any cardiac drug may be used in combination with Unger's compositions for their own intended clinical end point.

Thus, even though Unger does not explicitly use adenosine, it would have been obvious to one of ordinary skill in the art at the time of invention to use Unger's composition in combination with adenosine, as suggested by Unger's patent itself, because the ordinary artisan would have expected to see enhanced therapeutic results when Unger's composition is combined with adenosine.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shahnam Sharareh, PharmD whose telephone number is 703-306-5400. The examiner can normally be reached on 8:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Minna Moezie can be reached on 703-308-4612. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1123.

RUSSELL TRAVERS
PRIMARY EXAMINER
GROUP 1200